Serotonergic 5-HT(1A) receptor agonist (8-OH-DPAT) ameliorates impaired micturition reflexes in a chronic ventral root avulsion model of incomplete cauda equina/conus medullaris injury.

Journal: Exp Neurol

Publication Year: 2013

Authors: Huiyi H Chang, Leif A Havton

PubMed link: 23099413

Funding Grants: Repair of Conus Medullaris/Cauda Equina Injury using Human ES Cell-Derived Motor Neurons

Public Summary:
Injuries to the spinal cord and associated nerve roots may cause complete or partial lesions to the affected nervous structures. We developed an incomplete injury model in the form of a one-sided injury to lumbosacral roots in the rat. This injury resulted in detectable impairments of bladder function. Bladder pressure recordings and electrical activity recordings from the external urethra sphincter muscle showed that a pharmacological approach can improve bladder function after such injuries in rats. Specifically an experimental drug (8-OH-DPAT), which stimulates receptors normally activated by the brain neurochemical, serotonin, was able to improve voiding reflexes. We conclude that new treatments targeting serotonin mechanisms may improve bladder function after incomplete injuries to the lumbosacral nerve roots and spinal cord.

Scientific Abstract:
Trauma to the thoracolumbar spine commonly results in injuries to the cauda equina and the lumbosacral portion of the spinal cord. Both complete and partial injury syndromes may follow. Here, we tested the hypothesis that serotonergic modulation may improve voiding function after an incomplete cauda equina/conus medullaris injury. For this purpose, we used a unilateral L5-S2 ventral root avulsion (VRA) injury model in the rat to mimic a partial lesion to the cauda equina and conus medullaris. Compared to a sham-operated series, comprehensive urodynamic studies demonstrated a markedly reduced voiding efficiency at 12 weeks after the VRA injury. Detailed cystometrogram studies showed injury-induced decreased peak bladder pressures indicative of reduced contractile properties. Concurrent external urethral sphincter (EUS) electromyography demonstrated shortened burst and prolonged silent periods associated with the elimination phase. Next, a 5-HT(1A) receptor agonist, 8-hydroxy-2-(di-n-propylamino)-tetralin (8-OH-DPAT), was administered intravenously at 12 weeks after the unilateral L5-S2 VRA injury. Both voiding efficiency and maximum intravesical pressure were significantly improved by 8-OH-DPAT (0.3-1.0 mg/kg). 8-OH-DPAT also enhanced the amplitude of EUS tonic and bursting activity as well as duration of EUS bursting and silent period during EUS bursting. The results indicate that 8-OH-DPAT improves voiding efficiency and enhances EUS bursting in rats with unilateral VRA injury. We conclude that serotonergic modulation of the 5-HT(1A) receptor may represent a new strategy to improve lower urinary tract function after incomplete cauda equina/conus medullaris injuries in experimental studies.